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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/726,692	12/04/2003	Louis V. Kirchhoff	21311A	5808

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Stevens, Davis, Miller & Mosher, LLP
Suite 850
1615 L Street, NW
Washington, DC 20036-5622

EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 07/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/726,692	KIRCHHOFF ET AL.	
	Examiner	Art Unit	
	Padmavathi v. Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-5 and 12-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-11 and 18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following groups of invention is required under 35 U.S.C. 121:

I. Claims 1-5 drawn to recombinant plasmid DNA classified in class 536, subclass 23.7.

II. Claims 6-11 drawn to polypeptide and a kit comprising said polypeptide classified in class 530, 435 subclass 350, 975 respectively

III Claims 12-17 drawn to a method for detecting the presence of anti-*Trypanosoma cruzi* antibodies in a sample classified in class 435, subclass 7.22.

2. The inventions are distinct, each from the other because of the following reasons:

Group I is directed to DNA which consists of nucleic acids, Groups II is directed to polypeptides, which are made of amino acids. These products are different to each other structurally, biochemically and functionally and are drawn to patentably distinct inventions which have materially different physical and chemical properties and structures.

3. Invention II is related to invention III as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the protein of Group II can be used in immunoaffinity chromatography method for purifying antibodies and need not be used in the invention III.

4. Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, the literature and sequence searches required for each of the Groups are not required for another of the Groups, restriction for examination purposes as indicated is proper.

5. During a telephone conversation with Thomas P Pavelko on 4/13/04 a provisional election was made with traverse to prosecute the invention of Group II, claims 6-11. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-5 and 12-17 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Amendment

7. Applicants amendment filed on 4/13/04 is acknowledged.

Status of claims

8. New Claims 18-20 have been added.

Claims 1-20 are pending.

Claims 6-11 and newly added claims 18-20 are under investigation as an elected invention, said election made on 4/13/04.

Claims 1-5 and 12-17 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected group.

Priority

9. This application claims domestic priority under 35 U.S.C. 119(e) to Provisional Application 60/430654 filed on 12/04/2002.

Information Disclosure Statement

10. No Information Disclosure Statement (IDS) has been filed in this application.

Drawings

11. The drawings filed on 12/04/03 are accepted by the examiner.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 6-11 and 18-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6- 11 and 18-20 are indefinite in the recitation of Ag15, FP3, FP4, FP5, FP6, FP7, FP8, FP9 and FP10. These relative terms in claims renders the claim indefinite. They appear to be combination of various recombinant proteins. Recitation of the terms Ag15, FP3, FP4, FP5, FP6, FP7, FP8, FP9 and FP10 appear to be lab designations for recombinant fusion proteins. Since this is merely a lab designation, such terminology change from lab to lab or the same designation can be used for totally different polypeptides or cell lines or antibodies. Therefore, recitation of Ag15, FP3, FP4, FP5, FP6, FP7, FP8, FP9 and FP10 must be designated either by structural properties or sequence identification numbers or identified by ATCC numbers.

In claims 6 and 8, the abbreviation " Ag15, FP3, FP4, FP5. FP6, FP7, FP8, FP9 and FP10" is used without definition upon their first appearance in the claims.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 6, 7-11 and 18-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Kirchhoff et al U.S.Patent: 5,876,734.

Claim 6 is drawn to a recombinant polypeptide comprising a sequence corresponding to one of FP3, FP4, FP6, FP7, FP8 and FP10. Claims 7-11 and 18-20 are drawn to a kit comprising a first recombinant polypeptide comprising a sequence corresponding to one of FP3, FP4, FP6, FP7, FP8 and FP10, and a second recombinant polypeptide. Wherein the second polypeptide comprises a sequence corresponding to one selected from the group consisting of Ag15, FP3, FP4, FP5, FP6, FP7 FP8, FP9 and FP10, wherein the first recombinant polypeptide is different from the second recombinant polypeptide, wherein the first recombinant polypeptide is FP4 and the second recombinant polypeptide is FP6, wherein the third recombinant polypeptide selected from the group consisting of Ag15, FP3, FP4, FP5, FP6, FP7, FP8, FP9 and FP1û, wherein the first recombinant polypeptide, the second recombinant polypeptide and the recombinant polypeptide are different, wherein the first recombinant polypeptide corresponds to FP4, the second recombinant polypeptide corresponds to FP6 and the third polypeptide corresponds to FPI0, wherein the first polypeptide is FP3, the second polypeptide is FP6, and third recombinant polypeptide FPIO.

The examiner is interpreting the claims broadly because the product recombinant polypeptide comprising a sequence, which corresponds to FP3, FP4 etc does not set forth the structure, source, property and function of the product. Therefore, the following rejections are applied.

Kirchhoff et al disclose a recombinant polypeptide comprising a sequence (see SEQ.ID.NO: 10, column 6, lines 49-65 and figure 2E) encoded by 1396-1419 that corresponds to FP3 and thus read on claim 6. The prior art also disclose a kit comprising said polypeptide FP3 (column 3, lines 5-15 and column 6, lines 49-65, figure 2E). The kit further comprises a second recombinant protein comprising a sequence encoded by nucleotides 1672-1695 and 682-1671 of SEQ.ID.NO: 1 (see column 3, lines 5-15 and column 6, lines 20-25) corresponding to Ag15 and FP6 respectively. The kit further comprises a third recombinant polypeptide encoded by nucleotides 664-924 comprising a sequence that corresponds to FP10 (see, column 6, lines 40-42 and SEQ.ID.NO: 6 and figure 2 C) The first, second and third recombinant proteins are different to each other. The prior art anticipated the claimed invention.

16. Claim 6 is rejected under 35 U.S.C. 102(b) as being anticipated by Webb et al J. Biol Chem. 1998 May 22: 273(21): 13339-46.

Claim 6 is drawn to a recombinant polypeptide comprising a sequence corresponding to one of FP3, FP4, FP6, FP7, FP8 and FP10.

Webb et al disclose a recombinant fusion protein comprising a sequence (see under preparations of constructs on page 3340, right column, first two paragraphs and figure1) corresponding to FP3 from 614-797. The prior art anticipated the claimed invention.

17. Claims 6, 7, 8 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Browning et al U.S.Patent: 6,171,589.

Claim 6 is drawn to a recombinant polypeptide comprising a sequence corresponding to one of FP3, FP4, FP6, FP7, FP8 and FP10. Claims 7, 8 and 18 are drawn to a kit comprising: a first recombinant polypeptide comprising a sequence corresponding to one of FP3, FP4, FP6, FP7, FP8 and FP10, and a second recombinant polypeptide, wherein the second polypeptide comprises a sequence corresponding to one selected from the group consisting of Ag15, FP3, FP4, FP5, FP6. FP7 FP8, FP9 and FP10, wherein the first recombinant polypeptide is different from the second recombinant polypeptide,

Browning discloses recombinant polypeptides FP3 and FP4 and a kit comprising said polypeptides (see column 19, lines, 44-49 and Table 5). The kit and first recombinant protein comprise a sequence that corresponds to FP3 from position 887-962 of SEQ.ID.NO: 2 and a second recombinant protein of the kit, FP4 from position 969-1029 of SEQ.ID.NO: 2 (see column 19, lines, 44-49 and Table 5). The first and second proteins are different to each other. The prior art anticipated the claimed invention.

18. Claims 6-11 and 18-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Rico et al 1996, Journal of Dermatological Science 12: 238-245.

Claims have been discussed in Para # 15.

Kit claims are treated as product claims as kit is no different from the recombinant product claims

Rico et al disclose a recombinant fusion protein comprising a sequence corresponding to FP3 from 1003-1193, (see under Methods: fusion protein production, page 239, right column through page 240, left column and figure1) and a second recombinant protein comprising a sequence corresponding to FP7 from position 1623-1812. The first and second proteins are different to each other. The prior art also teaches other recombinant proteins such as FP9, FP16-8, and Fp16-1. All these polypeptides (antigen AG 16-1 etc) have been used in an immunoassay for epitope mapping of sera for bullous pemphigoid to fusion proteins target antigens BPAG1 and 2. The prior art clearly teaches significant reactivity of sera to more than one recombinant protein and different sera from different continents such as US and Japan would react to different recombinant proteins (see abstract) in an immunoassay (i.e., ELISA). Thus the prior art teaches use of more than one target recombinant protein (see abstract, Tables1-2 and figures 1-2) is necessary in epitope mapping of the target antigen. The prior art anticipated the claimed invention.

Relevant Prior Art

19. The prior art made of record and not relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

A. Burns et al Proc Natl Acad Sci U S A. 1992 February 15; 89(4): 1239–1243 teach immunodominant protein with a repetitive epitope from the protozoan Trypanosoma cruzi, the causative agent of Chagas disease. The identified 10-amino acid repeat is present within a high-molecular-weight trypomastigote antigen that appears specific to and conserved among T. cruzi isolates. More importantly, greater than 95% of T. cruzi infection sera, including both chronic and acute Chagas disease, contained elevated levels of antibody to a 15-amino acid synthetic peptide bearing the repetitive B-cell epitope. Considering the wide diversity of T. cruzi parasites, as well as the broad spectrum of clinical manifestations of Chagas disease, such a prevalent immune response among patients is significant and applicable to the control of Chagas disease through the diagnosis of T. cruzi infection.

B. SwissProt-42, Acession number: P81306 disclose recombinant protein LKEKAK.

C. Engman DM J. Biol. Chem. 1989 Nov 5; 264(31): 18627-31 teach a 24-kDa protein of Trypanosoma cruzi, the protozoan parasite that causes Chagas' disease, is recognized by antisera from both humans and experimental animals infected with this organism. Near its C terminus are two regions that have sequence similarity with several Ca2+-binding proteins and that conform to the "E-F hand" Ca2+-binding structure. The protein's low Ca2+-binding capacity (less than 2 mol of Ca2+/mol of protein) and high Ca2+-binding affinity (apparent Kd less than 50 microM Ca2+) are consistent with binding of Ca2+ via the E-F hand structures. Immunofluorescence assays using a mouse antiserum directed against the fusion protein localized the native protein to the trypanosome's flagellum. The protein's abundance, Ca2+-binding property, and flagellar localization suggest that it participates in molecular processes associated with the high motility of the parasite.
D. Otsu et al Mol Biochem Parasitol. 1993 Feb;57(2):317-30 teach antigenic proteins having repetitive domains. In earlier work we identified a partial length cDNA, designated TCR27, encoding approx. 26 copies of a 14-amino acid repeat and a unique 61-amino acid C-terminal region. The interrupted TCR27-2 gene was not impaired biologically suggests that the length of the repetitive region of the TCR27 protein is not a critical factor for survival.
E. Cotrim et al Mol Biochem Parasitol. 1995 Apr; 71(1): 89-98 teach the gene encoding an immunodominant repetitive antigen (flagellar antigen) associated to the cytoskeleton of Trypanosoma cruzi. The genomic organization and expression of the gene encoding a high molecular mass (300 kDa) repetitive antigen associated with the cytoskeleton of Trypanosoma cruzi. Protease digestion of the native protein, restriction analysis of genomic DNA and sequencing of genomic and cDNA clones indicated that most of the protein is built up by tandemly arranged, nearly identical repeats of 68 amino acids. The gene size was estimated to be approx. 9.4 kb based on the sizes of the transcript and the native protein. The nucleotide sequence conservation among the repeats indicates that selective sequence homogenization, presumably through gene conversion, maintained the amino-acid sequence conservation. Two duplicated allelic forms of this gene were mapped in fragments of about 20 kb. In some strains an additional allele was located in a fragment of 9.4 kb, suggesting that this repetitive antigen is a structural protein which could be involved in the attachment of the flagellum to the cell body.
F. Hoft et al Infect Immun. 1989 July; 57(7): 1959–1967 teach Trypanosoma cruzi cDNA expression library with human and rabbit anti-T. cruzi sera. The identified cDNA clones that encode polypeptides containing tandemly arranged repeats which are 6 to 34 amino acids in length. The peptide repeats encoded by these cDNAs varied markedly in sequence, copy number, and location relative to the polyadenylation site of the mRNAs from which they were derived. The repeats were specific for T. cruzi, but in each case the sizes of the corresponding mRNAs and the total number of repeat copies encoded varied considerably among different isolates of the parasite. Expression of the peptide repeats was not stage specific. One of the peptide repeats occurred in a protein with an Mr of greater than 200,000 and one was in a protein of Mr 75,000 to 105,000.

G. Cooper R et al J Cell Biol. 1993 Jul; 122(1): 149-56 teach an immunodominant Trypanosoma cruzi surface glycoprotein which disrupts flagellum-cell adhesion. Null mutants of the Trypanosoma cruzi insect stage-specific glycoprotein GP72 were created by targeted gene replacement. Targeting plasmids were constructed in which the neomycin phosphotransferase and hygromycin phosphotransferase genes were flanked by GP72 sequences. These plasmids were sequentially transfected into T. cruzi epimastigotes by electroporation. Southern blot

analyzes indicated that precise replacement of the two genes had occurred. No aberrant rearrangements occurred at the GP72 locus and no GP72 gene sequences had been translocated elsewhere in the genome. Western blots confirmed that GP72 is not expressed in these null mutants. The morphology of the mutants is dramatically different from wild-type. In both mutant and wild-type parasites, the flagellum emerges from the flagellar pocket. In the null mutant the normal attachment of the flagellum to the cell membrane of the parasite is lost.

H. Lesenechal M et al **Mol** Biochem Parasitol. 1997 Aug; 87(2): 193-204 teach a Trypanosoma cruzi genomic expression library was screened with a pool of sera obtained from chronic chagasic patients. The recombinant antigen (Tc40) isolated from this library reacted with a large number of serum samples of chronic chagas patients, suggesting that the presence of anti-Tc40 antibodies may be specifically associated to Chagas' disease. The full-length sequence of the Tc40 gene was determined after isolation of genomic and cDNA clones. The Tc40 cDNA includes a large open reading frame (2745 bp-long) that encodes a polypeptide of 100 kDa without any homology with previously described T. cruzi sequences. In contrast with other T. cruzi antigens whose immunodominant B-cell epitopes are composed by amino acid repetitive motifs, Tc40 does not show any amino acid repetition. Antibodies against the Tc40 recombinant protein reacted with three native polypeptides of 100, 41 and 38 kDa, which are tightly associated with membranes or cytoskeleton and expressed in all developmental stages of the parasite life cycle. A transcript of 3.9-kb was detected in Northern blot analysis, which is large enough to encode a 100-kDa polypeptide.

I. Gonzalez et al Nucleic Acids Res. 1985 Aug 26; 13(16): 5789-804 teach cloning and sequencing a gene which is organized in at least 20 nearly perfect tandem repeats of 940 base pairs. The 5' end of the mRNA has been sequenced by primer extension and found to contain a 35-nucleotide mini-exon (or spliced-leader) sequence that is ubiquitous in trypanosome mRNAs. This sequence, however, is not present in the tandem genomic repeats, which encode the exon containing the major portion of the mRNA.

J. Cooper et al Mol Biochem Parasitol. 1991 Nov; 49(1): 45-59 teach the Trypanosoma cruzi insect stage-specific antigen GP72 from epimastigotes and the amino acid sequences of peptide fragments determined. The characteristics of the encoded 62,600-Da protein, including a potential amino-terminal signal sequence, a hydrophobic carboxy-terminus, and a large number of potential O-glycosylation sites, are consistent with the properties of GP72. No sequence homologies were found in searches of DNA and protein data banks. GP72 is encoded by a single pair of non-telomeric allelic genes.

K. Lafaille et al I Mol Biochem Parasitol. 1989 Jun 15; 35(2): 127-36 teach antigenic proteins bearing repetitive epitopes. Trypanosoma cruzi genes were cloned in lambda gt11 and screened with an anti-trypomastigote antiserum. Two out of twelve clones were selected in view of their reactivity with human chagasic sera. One clone encodes a flagellar antigen (FRA) of more than 300 kDa, whereas the other corresponds to a roughly 225-kDa cytoplasmic antigen (CRA). The flagellar antigen is present in both epimastigotes and trypomastigotes, but the cytoplasmic antigen is not found in trypomastigotes. The CRA clone is entirely composed of at least 23 copies of a 42-bp repeat and the FRA gene contains at least 14 copies of a 204-bp

motif. The FRA gene hybridizes to a RNA of about 10 kb, while the CRA gene detects a transcript of 5.2 kb.

L. Gruber et al Exp Parasitol. 1993 Feb; 76(1): 1-12 teach two clones, B12 and B13, containing inserts of 350 and 600 bp, respectively were isolated. Sequencing data indicated that both clones present a pattern of tandemly repeated nucleotide units of 60 bp for B12 and 36 bp for B13. Southern blot analysis suggests that both corresponding genes exist as a single copy. The inserts of both recombinants were subcloned in the vector pMSgt11, in phase with the lacZ gene. Recombinant proteins were affinity purified on pAPTG-agarose columns and employed to immunize rabbits, as well as to immunoselect human chagasic antibodies. By Western blot, antibodies to B12 reacted with bands of 230 kDa in trypomastigotes and 200 kDa in epimastigotes, while those to B13 identified bands of 140 and 116 kDa in trypomastigotes and epimastigotes. Immunoprecipitation of radioiodinated parasites revealed that the 140-kDa antigen recognized by antibodies to B13 is located on the membrane of trypomastigotes but not epimastigotes. The potential application of either recombinant antigen in the serological diagnosis of Chagas' disease was evaluated initially by RIA. It was observed that B13 presents a very good performance with sensitivity of 97%. For B12, the corresponding value was 82%. The reactivity to B13 was also evaluated by ELISA tests run in parallel with conventional serological reactions for Chagas' disease. Analysis of 209 serum samples indicates that B13 presents similar or even better performance in relation to the use of total epimastigote antigens, making it a promising candidate for the diagnosis of Chagas' disease.

M. Affranchino et al FEBS Lett 1991; 280:316-320 teach Trypanosoma cruzi antigens we examined the gene structure and transcription properties of the major shed trypomastigote antigen (SAPA). SAPA is encoded by a small family of at lest 6 genes which differ mainly in the length of a repeat region made up of tandemly arranged 36-bp repeat units. SAPA genes are transcribed in the infective form of the parasite.

N. Kerner et al Experimental Parasitology 1991,.7344):451-459 teach K17 recombinant protein and antibodies to a MAP (microtubule associated like protein) in chronic Chagas' disease cross-react with mammalian cytoskeleton.

O. Virreira et al Am. J. Trop. Med. Hyg, 68(5), 2003, pp. 574-582 teach the polymerase chain reaction (PCR) is a potentially interesting diagnostic tool for detecting congenital *Trypanosoma cruzi* infection at birth.

P. Stijlemans et al J. Biol. Chem., Vol. 279, Issue 2, 1256-1261, January 9, 2004 teach antigen variation is a successful defense system adopted by several infectious agents to evade the host immune response. The principle of this defense strategy in the African trypanosome paradigm involves a dense packing of variant surface glycoproteins (VSG) exposing only highly variable and immuno-dominant epitopes to the immune system, whereas conserved epitopes become inaccessible for large molecules. Reducing the size of binders that target the conserved, less-immunogenic, cryptic VSG epitopes forms an obvious solution to combat these parasites. This goal was achieved by introducing dromedary Heavy-chain antibodies. We found that only these unique antibodies recognize epitopes common to multiple VSG classes. After

phage display of their antigen-binding repertoire, we isolated a single domain antibody fragment with high specificity for the conserved Asn-linked carbohydrate of VSG. In sharp contrast to labeled concanavalin-A that stains only the flagellar pocket where carbohydrates are accessible because of less dense VSG packing, the single domain binder stains the entire surface of viable parasites, irrespective of the VSG type expressed. This corroborates the idea that small antibody fragments, but not larger lectins or conventional antibody fragments, are able to penetrate the dense VSG coat to target their epitope. The diagnostic potential of this fluorescently labeled binder was proven by the direct, selective, and sensitive detection of parasites in blood smears. The employment of this binder as a molecular recognition unit in immuno-toxins designed for trypanosomosis therapy becomes feasible as well. This was illustrated by the specific trypanolysis induced by an antibody::β-lactamase fusion activating a prodrug.

Q. Daley et al , Clin. Diagn. Lab. Immunol., March 1, 2005; 12(3): 380 – 386 teach Heavy-Chain Immunoglobulins in New World Camelids. Of the three immunoglobulin G (IgG) isotypes described to occur in camelids, IgG2 and IgG3 are distinct in that they do not incorporate light chains. These heavy-chain antibodies (HCAbs) constitute approximately 50% of the IgG in llama serum and as much as 75% of the IgG in camel serum.
Isotype-specific mouse monoclonal antibodies (MAbs) were produced in order to investigate the roles of HCAbs in camelid immunity. Seventeen stable hybridomas were cloned, and three MAbs that were specific for epitopes on the γchains of llama IgG1, IgG2, or IgG3 were characterized in detail. Affinity chromatography revealed that each MAb bound its isotype in solution in llama serum. The antibodies bound to the corresponding alpaca IgGs, to guanaco IgG1 and IgG2, and to camel IgG1. Interestingly, anti-IgG2 MAbs bound three heavy-chain species in llama serum, confirming the presence of three IgG2 sub isotypes. Two IgG2 sub isotypes were detected in alpaca and guanaco sera. The MAbs detected llama serum IgGs when they were bound to antigen in enzyme-linked immunosorbent assays and were used to discern among isotypes induced during infection with a parasitic nematode.

Remarks

20 No claims are allowed.

Conclusion

21. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Right Fax number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Padma Baskar Ph.D.

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600